



## Generic DB Entry Retrieval

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ID      CBBONT1      standard; DNA; PRO; 4199 BP.
XX
AC      L35496;
XX
SV      L35496.1
XX
DT      23-AUG-1994 (Rel. 40, Created)
DT      04-MAR-2000 (Rel. 63, Last updated, Version 3)
XX
DE      Clostridium botulinum proteolytic type F neurotoxin botT/F gene, complete
DE      cds, and nontoxic-nonhaemagglutinin (ntnH) gene, 3' end.
XX
KW      botT/F gene; neurotoxin type F; nontoxic-nonhaemagglutinin; ntnH gene.
XX
OS      Clostridium botulinum
OC      Bacteria; Firmicutes; Clostridia; Clostridiales; Clostridiaceae;
OC      Clostridium.
XX
RN      [1]
RP      1-4199
RA      Elmore M.J., Bodsworth N.J., Whelan S.M., Minton N.P. ;
RT      "The complete nucleotide sequence of the gene coding for proteolytic type
RT      neurotoxin of Clostridium botulinum";
RL      Unpublished.
XX
DR      SPTREMBL; Q45850; Q45850.
DR      SPTREMBL; Q57236; Q57236.
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FT          /note="putative"
FT          /transl_table=11
FT          /gene="ntnH"
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FT          /note="putative"

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FT          /function="vertebrate neurotoxin"
FT          /product="neurotoxin type F"
FT          /protein_id="AAA23210.1"
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L1 ANSWER 13 OF 17 MEDLINE  
AN 97016817 MEDLINE  
DN 97016817 PubMed ID: 8863443  
TI Organization and phylogenetic interrelationships of genes encoding components of the botulinum toxin complex in proteolytic Clostridium botulinum types A, B, and F: evidence of chimeric sequences in the gene encoding the nontoxic nonhemagglutinin component.  
AU East A K; Bhandari M; Stacey J M; Campbell K D; Collins M D  
CS Department of Microbiology, Institute of Food Research, Reading, Berkshire, United Kingdom.. alison.east@bbsrc.ac.uk  
SO INTERNATIONAL JOURNAL OF SYSTEMATIC BACTERIOLOGY, (1996 Oct) 46 (4) 1105-12.  
Journal code: 0042143. ISSN: 0020-7713.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
OS GENBANK-X78230; GENBANK-X87974; GENBANK-X92973; GENBANK-X96491; GENBANK-X96492; GENBANK-X96493; GENBANK-X96494  
EM 199611  
ED Entered STN: 19961219  
Last Updated on STN: 19980206  
Entered Medline: 19961115  
AB The cluster of genes encoding components of the **botulinum neurotoxin** (BoNT) complex was mapped in proteolytic (group I) Clostridium botulinum strains encoding BoNT types A, B, and F. Two different arrangements of genes were found: type A strain 62A and type B strain NCTC 7273 have similar organizations of genes encoding BoNT, the nontoxic nonhemagglutinin component (NTNH), hemagglutinin components, and P-21; **type F** strain Langeland has genes encoding BoNT, NNTNH, and P-21, and a previously unidentified open reading frame encoding a protein of 416 amino acids. A group of type A strains typified by infant strain Kyoto-F, which is unlike type A strain 62A, lacks genes for hemagglutinin components and exhibits an organization similar to that of **type F**. Sequencing and pairwise analysis revealed the presence of possible chimeric sequences in some NNTNH genes of proteolytic C. botulinum. Discordance in genealogical trees derived from different regions of the NNTNH genes was observed which could be symptomatic of recombination and which may indicate that the NNTNH gene represents a hot spot for such events within the cluster of genes encoding the BoNT complex. It is also evident that the phylogenetics of the NNTNH gene, which is linked to the gene encoding BoNT, does not mirror the evolutionary history of the BoNT, upon which the C. botulinum species complex is defined and subdivided.

L1 ANSWER 14 OF 17 MEDLINE  
AN 94297488 MEDLINE  
DN 94297488 PubMed ID: 7764998  
TI Conserved structure of genes encoding components of **botulinum neurotoxin** complex M and the sequence of the gene coding for the nontoxic component in nonproteolytic Clostridium botulinum **type F**.  
AU East A K; Collins M D  
CS Department of Microbiology, Institute of Food Research, Reading Laboratory, UK.  
SO CURRENT MICROBIOLOGY, (1994 Aug) 29 (2) 69-77.  
Journal code: 7808448. ISSN: 0343-8651.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Biotechnology  
EM 199408

ED    Entered STN: 19950809  
Last Updated on STN: 19970203  
Entered Medline: 19940810  
AB    For investigation of the genes of proteins associated in vivo with **botulinum neurotoxin** (BoNT), polymerase chain reaction (PCR) experiments were carried out with oligonucleotide primers designed to regions of the nontoxic-nonhemagglutinin (NTNH) gene of Clostridium botulinum type C. The primers were used to amplify a DNA fragment from genomic DNA of C. botulinum types A, B, E, F, G and toxigenic strains of Clostridium barati and Clostridium butyricum. The amplified product from all of these strains hybridized with an internal oligonucleotide probe, whereas all nontoxigenic clostridia tested gave no PCR product and showed no reaction with the probe. The NNTNH gene was shown to be located upstream of the gene encoding BoNT, thereby revealing a conserved structure for genes encoding the proteins of the M complex of the progenitor botulinum toxin in these organisms. The sequence of the NNTNH gene of nonproteolytic C. botulinum **type F** was determined by PCR amplification and sequencing of overlapping cloned fragments. NNTNH/F showed 71% and 61% identity with NNTNH of C. botulinum type E and type C respectively.

L1    ANSWER 15 OF 17       MEDLINE  
AN    93012902           MEDLINE  
DN    93012902           PubMed ID: 1398040  
TI    Sequence of the gene encoding **type F** neurotoxin of Clostridium botulinum.  
AU    East A K; Richardson P T; Allaway D; Collins M D; Roberts T A; Thompson D E  
CS    Department of Microbiology, AFRC Institute of Food Research, Reading, UK.  
SO    FEMS MICROBIOLOGY LETTERS, (1992 Sep 15) 75 (2-3) 225-30.  
Journal code: 7705721. ISSN: 0378-1097.

CY    Netherlands  
DT    Journal; Article; (JOURNAL ARTICLE)  
LA    English  
FS    Priority Journals  
OS    GENBANK-M92906  
EM    199211  
ED    Entered STN: 19930122  
Last Updated on STN: 19970203  
Entered Medline: 19921119  
AB    Primers designed to conserved regions of botulinum and tetanus clostridial toxins were used to amplify DNA fragments from non-proteolytic Clostridium botulinum **type F** (202F) DNA using polymerase chain reaction technology. The fragments were cloned and the complete nucleotide sequence of the gene encoding **type F** toxin determined. Analysis of the nucleotide sequence demonstrated the presence of an open frame encoding a protein of 1274 amino acids, similar to other **botulinum neurotoxins**. Upstream of the toxin gene is the end of an open reading frame which encodes the C-terminus of a protein with homology to non-toxic-non-hemagglutinin component of type C progenitor toxin.

L1    ANSWER 16 OF 17       MEDLINE  
AN    90262533           MEDLINE  
DN    90262533           PubMed ID: 2188647  
TI    Botulinum **type F** neurotoxin. Large-scale purification and characterization of its binding to rat cerebrocortical synaptosomes.  
AU    Wadsworth J D; Desai M; Tranter H S; King H J; Hambleton P; Melling J; Dolly J O; Shone C C  
CS    Department of Biochemistry, Imperial College of Science and Technology, London, U.K.  
SO    BIOCHEMICAL JOURNAL, (1990 May 15) 268 (1) 123-8.

Journal code: 2984726R. ISSN: 0264-6021.  
CY ENGLAND: United Kingdom  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199006  
ED Entered STN: 19900720  
Last Updated on STN: 19970203  
Entered Medline: 19900628  
AB 1. A large-scale purification procedure has been developed for Clostridium botulinum **type F** neurotoxin. Commencing with 160 litres of bacterial culture, 101 mg of purified **type F** neurotoxin with a specific toxicity of  $2 \times 10(7)$  mouse LD<sub>50</sub> (median lethal dose).mg<sup>-1</sup> were obtained. 2. Purified **type F** neurotoxin was labelled to high specific radioactivity (900-1360 Ci/mmol) without loss of biological activity using a chloramine-T procedure. Of the two neurotoxin subunits, the heavy chain was preferentially radiolabelled. 3. Radiolabelled **type F** neurotoxin displayed specific saturable binding to rat synaptosomes. At least two pools of acceptors were evident: a low content of high-affinity acceptors sites [KD approximately 0.15 nM; B<sub>max</sub> (maximal binding) 20 fmol/mg] and a larger pool of lower-affinity sites (KD greater than 20 nM; B<sub>max</sub> greater than 700 fmol/mg). Both pools of acceptors were sensitive to trypsin and neuraminidase treatment, which suggests that protein and sialic acid residues are components of the synaptosomal acceptors. 4. Experiments investigating competition among **botulinum neurotoxin** types A, B, E and F for acceptors on rat brain synaptosomes showed that **type F** neurotoxin binds to acceptor molecules which are completely distinct from those of the other three neurotoxins.  
L1 ANSWER 17 OF 17 MEDLINE  
AN 84018414 MEDLINE  
DN 84018414 PubMed ID: 6353671  
TI Amino acid composition of Clostridium botulinum **type F** neurotoxin.  
AU DasGupta B E; Rasmussen S  
NC NS 17742 (NINDS)  
SO TOXICON, (1983) 21 (4) 566-9.  
Journal code: 1307333. ISSN: 0041-0101.  
CY ENGLAND: United Kingdom  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 198311  
ED Entered STN: 19900319  
Last Updated on STN: 19970203  
Entered Medline: 19831123  
AB To develop reliable data on the amino acid composition of **type F** **botulinum neurotoxin**, three batches of the neurotoxin were analyzed. Each batch was isolated from a separate neurotoxin producing bacterial culture. Two batches had inoculum from one source and the other batch one from a different source. Two batches of the neurotoxin were purified by the same method and one was purified by a different method. The neurotoxin preparations were found comparable in purity and similar in amino acid composition. The best estimate of number of amino acid residues per neurotoxin molecule (mol. wt. 155,000) was:  
Asp218 Thr80 Ser105 Glu128 Pro47 Gly69 Ala47 Val172 Cys9 Met14 Ile128  
Leu104 Tyr86 Phe60 Lys90 His13 Arg51 Trp23.

=>

L2 ANSWER 7 OF 10 MEDLINE  
AN 95179082 MEDLINE  
DN 95179082 PubMed ID: 7874084  
TI Inhibition of neurotransmitter release by clostridial neurotoxins correlates with specific proteolysis of synaptosomal proteins.  
AU Blasi J; Binz T; Yamasaki S; Link E; Niemann H; Jahn R  
CS Departament de Biologia Cel.lular i Anatomia Patologica, Facultat de Medicina, Universitat de Barcelona, Spain.  
SO JOURNAL OF PHYSIOLOGY, PARIS, (1994) 88 (4) 235-41.  
Journal code: 9309351. ISSN: 0928-4257.  
CY France  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199504  
ED Entered STN: 19950419  
Last Updated on STN: 19970203  
Entered Medline: 19950404  
AB Rat brain synaptosomes were used to study the effect of several clostridial neurotoxins on the neurotransmitter release. In this system the blockade of transmitter release correlated with the proteolytic activity of the toxins. Blockade of glutamate release was linked to selective proteolysis of one of the following synaptic proteins: synaptobrevin (BoNT/D, **BoNT/F**); SNAP-25 (BoNT/A, BoNT/E), or HPC-1/syntaxin (BoNT/C1). All the toxins used had an inhibitory effect on synaptosomes with the exception of **BoNT/F**. **BoNT/F** cleaved synaptobrevin in permeabilized synaptosomes but failed to produce the same effect on intact synaptosomes.

L2 ANSWER 8 OF 10 MEDLINE  
AN 94230352 MEDLINE  
DN 94230352 PubMed ID: 8175689  
TI Cleavage of members of the synaptobrevin/VAMP family by types D and F botulinal neurotoxins and tetanus toxin.  
AU Yamasaki S; Baumeister A; Binz T; Blasi J; Link E; Cornille F; Roques B; Fykse E M; Sudhof T C; Jahn R; +  
CS Department of Microbiology, Federal Research Center for Virus Diseases of Animals, Tubingen, Federal Republic of Germany.  
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1994 Apr 29) 269 (17) 12764-72.  
Journal code: 2985121R. ISSN: 0021-9258.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199406  
ED Entered STN: 19940620  
Last Updated on STN: 19970203  
Entered Medline: 19940606  
AB Tetanus toxin (TeTx) and the various forms of botulinal neurotoxins (BoNT/A to BoNT/G) potently inhibit neurotransmission by means of their L chains which selectively proteolyze synaptic proteins such as synaptobrevin (TeTx, BoNT/B, **BoNT/F**), SNAP-25 (BoNT/A), and syntaxin (BoNT/C1). Here we show that BoNT/D cleaves rat synaptobrevin 1 and 2 in toxified synaptosomes and in isolated vesicles. In contrast, synaptobrevin 1, as generated by in vitro translation, is only a poor substrate for BoNT/D, whereas this species is cleaved by **BoNT/F** with similar potency. Cleavage by BoNT/D occurs at the peptide bond Lys59-Leu60 which is adjacent to the **BoNT/F** cleavage site (Gln58-Lys59) and again differs from the site hydrolyzed by TeTx and BoNT/B (Gln76-Phe77). Cellubrevin, a recently

discovered isoform expressed outside the nervous system, is efficiently cleaved by all three toxins examined. For further characterization of the substrate requirements of BoNT/D, we tested amino- and carboxyl-terminal deletion mutants of synaptobrevin 2 as well as synthetic peptides. Shorter peptides containing up to 15 amino acids on either side of the cleavage site were not cleaved, and a peptide extending from Arg47 to Thr116 was a poor substrate for all three toxins tested. However, cleavability was restored when the peptide is further extended at the NH<sub>2</sub> terminus (Thr27-Thr116) demonstrating that NH<sub>2</sub> terminally located sequences of synaptobrevin which are distal from the respective cleavage sites are required for proteolysis. To further examine the isoform specificity, several mutants of rat synaptobrevin 2 were generated in which individual amino acids were replaced with those found in rat synaptobrevin 1. We show that a Met46 to Ile46 substitution drastically diminishes cleavability by BoNT/D and that the presence of Val76 instead of Gln76 dictates the reduced cleavability of synaptobrevin isoforms by TeTx.

L2 ANSWER 9 OF 10 MEDLINE  
AN 94013372 MEDLINE  
DN 94013372 PubMed ID: 8408542  
TI Gene probes for identification of the botulinal neurotoxin gene and specific identification of neurotoxin types B, E, and F.  
AU Campbell K D; Collins M D; East A K  
CS Reading Laboratory, Institute of Food Research, Agriculture and Food Research Council, United Kingdom.  
SO JOURNAL OF CLINICAL MICROBIOLOGY, (1993 Sep) 31 (9) 2255-62.  
Journal code: 7505564. ISSN: 0095-1137.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
OS GENBANK-X70814; GENBANK-X70815; GENBANK-X70816; GENBANK-X70817;  
GENBANK-X70818; GENBANK-X70819; GENBANK-X70820; GENBANK-X70821  
EM 199311  
ED Entered STN: 19940117  
Last Updated on STN: 19970203  
Entered Medline: 19931102  
AB A polymerase chain reaction method was developed for the specific detection of the botulinum neurotoxin (BoNT) gene of Clostridium botulinum. Degenerate oligonucleotide primers, designed from the nucleotide sequence of the heavy chain of the BoNT gene, amplified a specific fragment of approximately 1.1 kb from strains of C. botulinum toxin types A, B, E, F, and G and neurotoxin-producing strains of Clostridium barati and Clostridium butyricum, but no fragment was obtained from nontoxigenic strains. The fragments amplified from several strains of C. botulinum types B, E, and F were cloned in Escherichia coli and their nucleotide sequences were determined. Sequences within this region were used to design oligonucleotide probes specific for BoNT type B (BoNT/B), BoNT/E, and BoNT/F genes. An additional probe was designed for the detection of the BoNT/F gene of C. barati, which differed in sequence from BoNT/F genes of both proteolytic and nonproteolytic strains of C. botulinum.

L2 ANSWER 10 OF 10 MEDLINE  
AN 93012902 MEDLINE  
DN 93012902 PubMed ID: 1398040  
TI Sequence of the gene encoding type F neurotoxin of Clostridium botulinum.  
AU East A K; Richardson P T; Allaway D; Collins M D; Roberts T A; Thompson D E  
CS Department of Microbiology, AFRC Institute of Food Research, Reading, UK.  
SO FEMS MICROBIOLOGY LETTERS, (1992 Sep 15) 75 (2-3) 225-30.  
Journal code: 7705721. ISSN: 0378-1097.

CY Netherlands  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
OS GENBANK-M92906  
EM 199211  
ED Entered STN: 19930122  
Last Updated on STN: 19970203  
Entered Medline: 19921119  
AB Primers designed to conserved regions of botulinum and tetanus clostridial toxins were used to amplify DNA fragments from non-proteolytic Clostridium botulinum type F (202F) DNA using polymerase chain reaction technology. The fragments were cloned and the complete nucleotide sequence of the gene encoding type F toxin determined. Analysis of the nucleotide sequence demonstrated the presence of an open frame encoding a protein of 1274 amino acids, similar to other botulinum neurotoxins. Upstream of the toxin gene is the end of an open reading frame which encodes the C-terminus of a protein with homology to non-toxic-non-hemagglutinin component of type C progenitor toxin.

=>

The image shows the NCBI Protein search interface. At the top, there's a banner with the NCBI logo and the word "Protein". Below it is a search bar with "Search" and "Protein" dropdowns, and buttons for "Go" and "Clear". Navigation tabs include "Limits", "Preview/Index", "History", "Clipboard", and "Details". Below the search bar are buttons for "Display" (set to "default"), "Save" (as a "Text" file), "Add to Clipboard", and "Get Subsequence".

1: P10845. Botulinum neuroto...[gi:399133]

Links

**LOCUS** BXA1\_CLOBO 1296 aa linear BCT 15-JUN-2002  
**DEFINITION** Botulinum neurotoxin type A precursor (BoNT/A) (Bontoxilysin A) (BOTOX) [Contains: Botulinum neurotoxin A, light-chain; Botulinum neurotoxin A, heavy-chain].  
**ACCESSION** P10845  
**VERSION** P10845 GI:399133  
**DBSOURCE** swissprot: locus BXA1\_CLOBO, accession P10845;  
 class: standard.  
 extra accessions:P18639,P01561,created: Jul 1, 1989.  
 sequence updated: Jul 1, 1993.  
 annotation updated: Jun 15, 2002.  
 xrefs: gi: 40381, gi: 40382, gi: 144864, gi: 144865, gi: 1619251,  
 gi: 1619253, gi: 2160224, gi: 2160225, gi: 144880, gi: 551776, gi:  
279630, gi: 98562, pdb accession 3BTA  
 xrefs (non-sequence databases): MEROPS M27.002, InterPro IPR000395,  
 InterPro IPR000130, Pfam PF01742, PRINTS PR00760, ProDom PD001963,  
 PROSITE PS00142  
**KEYWORDS** Neurotoxin; Transmembrane; Hydrolase; Metalloprotease; Zinc;  
 Pharmaceutical; 3D-structure.  
**SOURCE** Clostridium botulinum.  
**ORGANISM** Clostridium botulinum  
 Bacteria; Firmicutes; Clostridia; Clostridiales; Clostridiaceae;  
 Clostridium.  
**REFERENCE** 1 (residues 1 to 1296)  
**AUTHORS** Thompson,D.E., Brehm,J.K., Oultram,J.D., Swinfield,T.J.,  
 Shone,C.C., Atkinson,T., Melling,J. and Minton,N.P.  
**TITLE** The complete amino acid sequence of the *Clostridium botulinum* type A neurotoxin, deduced by nucleotide sequence analysis of the encoding gene  
**JOURNAL** Eur. J. Biochem. 189 (1), 73-81 (1990)  
**MEDLINE** 90235864  
**PUBMED** 2185020  
**REMARK** SEQUENCE FROM N.A.  
 STRAIN=NCTC 2916  
**REFERENCE** 2 (residues 1 to 1296)  
**AUTHORS** Binz,T., Kurazono,H., Wille,M., Frevert,J., Wernars,K. and Niemann,H.  
**TITLE** The complete sequence of botulinum neurotoxin type A and comparison with other clostridial neurotoxins  
**JOURNAL** J. Biol. Chem. 265 (16), 9153-9158 (1990)  
**MEDLINE** 90264400  
**PUBMED** 2160960  
**REMARK** SEQUENCE FROM N.A.  
 STRAIN=62A  
**REFERENCE** 3 (residues 1 to 1296)  
**AUTHORS** East,A.K., Bhandari,M., Stacey,J.M., Campbell,K.D. and Collins,M.D.  
**TITLE** Organization and phylogenetic interrelationships of genes encoding components of the botulinum toxin complex in proteolytic *Clostridium botulinum* types A, B, and F: evidence of chimeric sequences in the gene encoding the nontoxic nonhemagglutinin

component  
JOURNAL Int. J. Syst. Bacteriol. 46 (4), 1105-1112 (1996)  
MEDLINE 97016817  
PUBMED 8863443  
REMARK SEQUENCE OF 1-65 FROM N.A.  
STRAIN=62A  
REFERENCE 4 (residues 1 to 1296)  
AUTHORS Betley,M.J., Somers,E. and DasGupta,B.R.  
TITLE Characterization of botulinum type A neurotoxin gene: delineation of the N-terminal encoding region  
JOURNAL Biochem. Biophys. Res. Commun. 162 (3), 1388-1395 (1989)  
MEDLINE 89350959  
PUBMED 2669749  
REMARK SEQUENCE OF 1-34 FROM N.A.  
STRAIN=Hall  
REFERENCE 5 (residues 1 to 1296)  
AUTHORS Fujita,R., Fujinaga,Y., Inoue,K., Nakajima,H., Kumon,H. and Oguma,K.  
TITLE Molecular characterization of two forms of nontoxic-nonhemagglutinin components of Clostridium botulinum type A progenitor toxins  
JOURNAL FEBS Lett. 376 (1-2), 41-44 (1995)  
MEDLINE 96096783  
PUBMED 8521962  
REMARK SEQUENCE OF 1-18 FROM N.A.  
STRAIN=Type A NIH  
REFERENCE 6 (residues 1 to 1296)  
AUTHORS Schmidt,J.J., Sathyamoorthy,V. and DasGupta,B.R.  
TITLE Partial amino acid sequence of the heavy and light chains of botulinum neurotoxin type A  
JOURNAL Biochem. Biophys. Res. Commun. 119 (3), 900-904 (1984)  
MEDLINE 84178501  
PUBMED 6370252  
REMARK SEQUENCE OF 1-16.  
REFERENCE 7 (residues 1 to 1296)  
AUTHORS Dasgupta,B.R., Foley,J. and Niece,R.  
TITLE Partial sequence of the light chain of botulinum neurotoxin type A  
JOURNAL Biochemistry 26, 4162-4162 (1987)  
REMARK SEQUENCE OF 1-46.  
REFERENCE 8 (residues 1 to 1296)  
AUTHORS DasGupta,B.R. and Dekleva,M.L.  
TITLE Botulinum neurotoxin type A: sequence of amino acids at the N-terminus and around the nicking site  
JOURNAL Biochimie 72 (9), 661-664 (1990)  
MEDLINE 91120847  
PUBMED 2126206  
REMARK SEQUENCE OF 1-5 AND 444-456.  
REFERENCE 9 (residues 1 to 1296)  
AUTHORS Sathyamoorthy,V., Dasgupta,B.R., Foley,J. and Niece,R.L.  
TITLE Botulinum neurotoxin type A: cleavage of the heavy chain into two halves and their partial sequences  
JOURNAL Arch. Biochem. Biophys. 266 (1), 142-151 (1988)  
MEDLINE 89024662  
PUBMED 3178218  
REMARK SEQUENCE OF 448-464 AND 872-895.  
REFERENCE 10 (residues 1 to 1296)  
AUTHORS Shone,C.C., Hambleton,P. and Melling,J.  
TITLE Inactivation of Clostridium botulinum type A neurotoxin by trypsin and purification of two tryptic fragments. Proteolytic action near the COOH-terminus of the heavy subunit destroys toxin-binding activity  
JOURNAL Eur. J. Biochem. 151 (1), 75-82 (1985)  
MEDLINE 85285016  
PUBMED 3896784  
REMARK SEQUENCE OF 448-482.

REFERENCE 11 (residues 1 to 1296)  
AUTHORS Schiavo,G., Santucci,A., Dasgupta,B.R., Mehta,P.P., Jontes,J.,  
Benfenati,F., Wilson,M.C. and Montecucco,C.  
TITLE Botulinum neurotoxins serotypes A and E cleave SNAP-25 at distinct  
COOH-terminal peptide bonds  
JOURNAL FEBS Lett. 335 (1), 99-103 (1993)  
MEDLINE 94063091  
PUBMED 8243676  
REMARK IDENTIFICATION OF SUBSTRATE.  
REFERENCE 12 (residues 1 to 1296)  
AUTHORS Binz,T., Blasi,J., Yamasaki,S., Baumeister,A., Link,E.,  
Sudhof,T.C., Jahn,R. and Niemann,H.  
TITLE Proteolysis of SNAP-25 by types E and A botulinal neurotoxins  
J. Biol. Chem. 269 (3), 1617-1620 (1994)  
JOURNAL 94124495  
MEDLINE 8294407  
PUBMED 8294407  
REMARK IDENTIFICATION OF SUBSTRATE.  
REFERENCE 13 (residues 1 to 1296)  
AUTHORS Rigoni,M., Caccin,P., Johnson,E.A., Montecucco,C. and Rossetto,O.  
TITLE Site-directed mutagenesis identifies active-site residues of the  
light chain of botulinum neurotoxin type A  
JOURNAL Biochem. Biophys. Res. Commun. 288 (5), 1231-1237 (2001)  
MEDLINE 21556941  
PUBMED 11700044  
REMARK MUTAGENESIS OF GLU-261; PHE-265 AND TYR-365.  
REFERENCE 14 (residues 1 to 1296)  
AUTHORS Lacy,D.B., Tepp,W., Cohen,A.C., DasGupta,B.R. and Stevens,R.C.  
TITLE Crystal structure of botulinum neurotoxin type A and implications  
for toxicity  
JOURNAL Nat. Struct. Biol. 5 (10), 898-902 (1998)  
MEDLINE 98455071  
PUBMED 9783750  
REMARK X-RAY CRYSTALLOGRAPHY (3.3 ANGSTROMS).  
COMMENT On or before Sep 14, 1993 this sequence version replaced gi:[115193](#),  
gi:[115174](#).

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collaboration between the Swiss Institute of Bioinformatics and  
the EMBL outstation - the European Bioinformatics Institute.  
The original entry is available from <http://www.expasy.ch/sprot>  
and <http://www.ebi.ac.uk/sprot>

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[FUNCTION] Inhibits acetylcholine release. The botulinum toxin  
binds with high affinity to peripheral neuronal presynaptic  
membrane, is then internalized by receptor-mediated endocytosis.  
The C-terminus of the heavy chain (H) is responsible for the  
adherence of the toxin to the cell surface while the N-terminus  
mediates transport of the light chain from the endocytic vesicle to  
the cytosol. After translocation, the light chain (L) hydrolyzes  
the 197-Gln-|-Arg-198 bond in SNAP-25, thereby blocking  
neurotransmitter release. Inhibition of acetylcholine release  
results in flaccid paralysis, with frequent heart or respiratory  
failure.

[CATALYTIC ACTIVITY] Limited hydrolysis of proteins of the  
neuroexocytosis apparatus, synaptobrevins, SNAP25 or syntaxin. No  
detected action on small molecule substrates.

[SUBUNIT] Disulfide-linked heterodimer of a light chain (L) and a  
heavy chain (H).

[SUBCELLULAR LOCATION] Secreted.

PHARMACEUTICAL: Available under the name BOTOX (Allergan) for the  
treatment of strabismus and blepharospasm associated with dystonia  
and cervical dystonia. Also used for the treatment of hemifacial  
spasm and a number of other neurological disorders characterized by  
abnormal muscle contraction.

[MISCELLANEOUS] There are seven antigenically distinct forms of

botulinum neurotoxin: Types A, B, C1, D, E, F, and G.  
[SIMILARITY] BELONGS TO PEPTIDASE FAMILY M27.  
[DATABASE] NAME=BOTOX product information Web site;  
WWW='http://www.botox.com/index.jsp?hp&productinfo'.  
[DATABASE] NAME=Protein Spotlight; NOTE=Issue 19 of February 2002;  
WWW='http://www.expasy.org/spotlight/articles/sptlt019.html'.

FEATURES Location/Qualifiers

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/db\_xref="taxon:1491"

gene 1..1296  
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/note="BNA; ATX"

Protein 1..1296  
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/EC\_number="3.4.24.69"

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/note="BOTULINUM NEUROTOXIN A, LIGHT-CHAIN."

Region 2  
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/region\_name="Conflict"  
/note="P -> Q (IN REF. 1)."

Region 27  
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/region\_name="Variant"  
/note="V -> A."

Site 223  
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Site 224  
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/site\_type="active"

Site 227  
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/site\_type="metal-binding"  
/note="ZINC (CATALYTIC)."

Site 262  
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Site 262  
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Site 266  
/gene="BOTA"  
/site\_type="mutagenized"  
/note="F->A: DECREASE IN ENZYMATIC ACTIVITY."

Site 366  
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Bond bond(430,454)  
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/bond\_type="disulfide"  
/note="INTERCHAIN."

Region 449..1296  
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/region\_name="Mature chain"  
/note="BOTULINUM NEUROTOXIN A, HEAVY-CHAIN."

Region 480

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/gene="BOTA"
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/note="POTENTIAL."
Region 876
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/note="T -> L (IN REF. 8)."
Region 892
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/region_name="Conflict"
/note="S -> K (IN REF. 8)."
Bond bond(1235,1280)
/gene="BOTA"
/bond_type="disulfide"

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121 stidtelkvi dtncinviqp dgsyrseeln lviigpsadi iqfecksfgh evlnltrngy
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421 glfefyklle vrgiitsktk sldkgynkal ndlcikvnnw dlffspsedn ftndlnkgee
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541 kkyeldkytm fhylraqefe hgksrialtn svneallnps rvytffssdy vkkvnkatea
601 amflgwveql vydftdetse vsttdkiadi tiiipyigpa lnignmlykd dfvgalifsg
661 avillefi pe iaipvlgtfa lvsyiankvl tvqtidnals krnekwddevy kyivtnwlak
721 vntqidlirk kmkealenqa eatkainyq ynqyteeekn ninfniddls sklnesinka
781 mininkflnq csvsylmnsm ipygvkrlled f daslk dall kyi ydnrgtl igqvdrlkdk
841 vnntlst dip fqlskyvdnq rllstf teyi kni ntsiln lryesnhlid lsryaskini
901 gskvnfdpid knqiqlfnle sskievilkn aivynsmyen fstsfwirip kyfnsislnn
961 eytiincmen nsgwkvslny geiwtlqdt qeikqrvvfk ysqminisdy inrwifvtit
1021 nnrlnnnskiy ingrlidqkp isnlgnihas nnimfkl dgc rdthryiwik yfnlfkeln
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1141 gsvmttniyl nsslyrgt kf iikkyasgnk dnivrnn drv yinvvvknke yrlatnasqa
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1261 lvasnwynrq ierssrtl gc swefipvddg wgerpl
//
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Revised: July 5, 2002.

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Sep 23 2002 19:33:30

ID Q57236 PRELIMINARY; PRT; 1278 AA.  
 AC Q57236; Q45863;  
 DT 01-NOV-1996 (TrEMBLrel. 01, Created)  
 DT 01-NOV-1996 (TrEMBLrel. 01, Last sequence update)  
 DT 01-OCT-2002 (TrEMBLrel. 22, Last annotation update)  
 DE Botulinum neurotoxin type F (BONT/F protein).  
 GN BONT/F.  
 OS Clostridium botulinum.  
 OC Bacteria; Firmicutes; Bacillus/Clostridium group; Clostridia;  
 OC Clostridiales; Clostridiaceae; Clostridium.  
 OX NCBI\_TaxID=1491;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RC STRAIN=NCTC 10281;  
 RA Hutson R.A., Collins M.D.;  
 RL Submitted (AUG-1995) to the EMBL/GenBank/DDBJ databases.  
 RN [2]  
 RP SEQUENCE FROM N.A.  
 RA Elmore M.J., Bodsworth N.J., Whelan S.M., Minton N.P.;  
 RL Submitted (AUG-1994) to the EMBL/GenBank/DDBJ databases.  
 RN [3]  
 RP SEQUENCE OF 635-1000 FROM N.A.  
 RC STRAIN=NCTC 1028;  
 RX MEDLINE=94013372; PubMed=8408542;  
 RA Campbell K., East A.K., Collins M.D.;  
 RT "Gene probes for identification of the botulinal neurotoxin gene and  
 specific identification of neurotoxin types B, E, and F.";  
 RL J. Clin. Microbiol. 31:2255-2262(1993).  
 RN [4]  
 RP SEQUENCE OF 1-27 FROM N.A.  
 RC STRAIN=LANGE LAND;  
 RX MEDLINE=98404102; PubMed=9732534;  
 RA East A.K., Bhandari M., Hielm S., Collins M.D.;  
 RT "Analysis of the botulinum neurotoxin type F gene clusters in  
 proteolytic and nonproteolytic Clostridium botulinum and Clostridium  
 barati.";  
 RL Curr. Microbiol. 37:262-268(1998).  
 DR EMBL; X81714; CAA57358.1; -.  
 DR EMBL; L35496; AAA23210.1; -.  
 DR EMBL; X70821; CAA50152.1; -.  
 DR EMBL; X99064; CAA67512.1; -.  
 DR HSSP; P10845; 3BTA.  
 DR MEROPS; M27.002; -.  
 DR InterPro; IPR000395; Bontoxilysin.  
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 DR Pfam; PF01742; Peptidase\_M27; 1.  
 DR PRINTS; PR00760; BONTOXILYSIN.  
 DR ProDom; PD001963; Bontoxilysin; 1.  
 DR PROSITE; PS00142; ZINC\_PROTEASE; UNKNOWN\_1.  
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